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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/389,782	09/03/1999	COLIN R. DUNSTAN	A-604	5852

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AMGEN INCORPORATED
MAIL STOP 27-4-A
ONE AMGEN CENTER DRIVE
THOUSAND OAKS, CA 91320-1799

EXAMINER	
HELMS, LARRY RONALD	
ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/389,782	Applicant(s) DUNSTAN ET AL.	
	Examin r Larry R. Helms	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

1. The request filed on 2/7/03 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/389782 is acceptable and a CPA has been established. An action on the CPA follows.

2. Claims 31-31 are pending.

Claims 21 and 22 have been amended.

3. Claims 21-31 are under examination.

4. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

5. The following Office Action contains some NEW GROUNDS of rejection.

Rejection Withdrawn

6. The rejection of claims 21-25, 26-31 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendment to the claims adding that the protein has activity of decreasing bone resorption.

7. The rejection of claim 23 under 35 U.S.C. 102(b) as being anticipated by Boyle et al (WO 97/23614, published 7/3/97, IDS #6) is withdrawn upon reconsideration.

8. The rejection of claims 21-31 under 35 U.S.C. 103(a) as being unpatentable over Mann et al (WO 98/28427, published 7/2/98, IDS #6) and further in view of Boyle et al (U.S. Patent 6,015,938, filed as a divisional with a filing date of 12/22/95) is withdrawn in view of the new ground of rejection.

Response to Arguments

9. The rejection of amended claim 21 under 35 U.S.C. 102(b) as being anticipated by Boyle et al (WO 97/23614, published 7/3/97, IDS #6) is maintained.

The response filed 2/7/02 and 9/27/02 has been carefully considered but is deemed not to be persuasive. The response of 9/27/02 states applicants have amended claim 21 to recite wherein the OPG protein comprises amino acids 22-401 as shown in Figure 2 (SEQ ID NO:2) and "the amendment was made solely to clarify that the claimed variants or fragments differ from OPG comprising residues 22-401" (see page 4 of response of 9/27/02). In response to this argument, it is unclear how the claimed fragments which comprise 22-401 of SEQ ID NO:2 is different from OPG comprising 22-401 of SEQ ID NO:2. Boyle et al clearly teach a fusion protein comprising an OPG variant 22-401 fused at its N-terminus to the C-terminus of the Fc protein (see page 105, lines 19-25) and it would be inherent that the protein has the activity of decreasing bone resorption.

The following is a NEW GROUND of rejection

Claim Rejections - 35 USC § 103

10. Claims 21-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boyle et al (WO 97/23614, published 7/3/97, IDS #6) as applied to claim 21 and further in view of Mann et al (WO 98/28427, published 7/2/98, IDS #6).

The claims are summarized as a protein comprising an FC-OPG fusion protein wherein the Fc is a variant or fragment and the OPG comprises 22-401 of SEQ ID NO:2 and the protein has activity of decreasing bone resprption , further claimed is an Fc with a cysteine at position 5 deleted or substituted, and the OPG comprises residues 22-185 to 293 of SEQ ID NO:2, a linker of glycine, alanine, serine, a fusion protein comprised of SEQ ID NO:5, 6, 7, 8, polyethylene glycol polymer attached to the N-terminus and compositions comprising such. For this rejection the intended use of decreasing bone resorption recited in claim 31 is given no patentable weight.

Boyle et al teach FC-OPG fusion proteins and the fusion protein comprises residues 22-401 of OPG (see page 105) and truncated variants of OPG (see Table 1) and the Fc region can have a linker linking the Fc and the OPG and fusions comprising PEG and OPG wherein PEG is at the N-terminal of OPG (see pages 140-143). Boyle et al does not teach modification of the Fc protein or covalent attachment of PEG to the N-terminal of the Fc-OPG fusion protein or the specific sequences of SEQ ID NO:5, 6, 7,8. These deficiencies are made up for in the teachings of Mann et al.

Mann et al teach fusion proteins comprising the Fc of SEQ ID NO:1 (see SEQ ID NO:9) and modifications to ablate the Fc receptor binding or complement binding (see page 8, lines 23-25) and many linkers, specifically the linker (Gly)7 (see page 9, lines 10-23) and polymers conjugated to proteins and pharmaceutical compositions

comprising such (see pages 15-31). Mann et al also teach the advantages of Fc fusions to proteins in general (see page 2-3) and the fusions of many proteins to Fc proteins (see pages 3-4).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the OPG protein as taught by Boyle et al and produce a fusion protein with the Fc protein or a modified Fc protein or with a linker as taught by Mann et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the OPG protein as taught by Boyle et al and produce a fusion protein with the Fc protein with a linker as taught by Mann et al because Boyle et al specifically teaches fusion proteins of OPG to Fc (Fc-OPG) wherein the OPG can comprise residues 22 to 180-401. In addition, one of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the OPG protein as taught by Boyle et al and produce a fusion protein with the Fc protein with a linker as taught by Mann et al because Mann et al teach fusion proteins of Fc and many therapeutically important proteins to achieve increased circulation times and Mann et al also teach modifications to the Fc protein to ablate certain functions and fusions with a linker. It would have been obvious to substitute any therapeutically important protein such as OPG for the OB protein of Mann et al given the teachings in Boyle et al that OPG is therapeutically important for bone resorption. It would also be obvious to produce the fusion protein because Boyle et al teach modifications at the N or C-terminal of OPG and as such one skilled in the art would conclude that any

orientation would be expected to work and in addition Boyle et al added a large polymer of PEG to the N-terminus of OPG and the OPG retained its activity (see Table 3). In addition, it would be obvious that a fusion protein of OPG and Fc with modifications as taught by Mann et al for a Fc protein and modifications as taught by Boyle et al for OPG would have the sequences recited in claim 7 and it would have been obvious that other linkers such as those recited in claim 25 can be used.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

The response filed 2/7/02 and 9/27/02 has been carefully considured but is deemed not to be persuasive. The response of 9/27/02 states that WO97/23614 discloses that carboxy-terminal truncated forms of OPG retain activity suggesting that it may be possible to make Fc fusions at the carboxy-terminus of OPG, however, there was no assurance that an Fc fusion at the amino terminus would result in active peptide (see page 4-5 of response). In response to this argument, Boyle et al specifically teach that a conjugation of a large molecule of PEG at the N-terminus of OPG resulted in an active protein and as such one skill in the art would reasonably conclude that molecules other that PEG can be conjugated to the N-terminus and still retain activity and in fact Boyle et al specifically teach Fc-OPG fusions.

Conclusions

11. No claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879